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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/110,720	07/07/98	BILLING-MEDEL	P 6130.US.P1

HM22/0609

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EXAMINER	
ZITOMER,S	
ART UNIT	**PAPER NUMBER**
1655	16
DATE MAILED:	06/09/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trad marks

Office Action Summary

Application No.	Applicant(s)
09/110,720	BILLING-MEDEL et al.
Examiner	**Group Art Unit**
Stephanie Zitomer	1655

☒ Responsive to communication(s) filed on *Mar 9, 2000*.

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-32 and 34-49* is/are pending in the application.

Of the above, claim(s) *1-10, 15-32, 34-37, and 40-44* is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *11-14, 38, 39, and 45-49* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Application status

1. The request filed on March 9, 2000 for a Continued Prosecution Application (CPA) under 37 CAR 1.53(d) based on parent Application No. 09/110,720 is acceptable and a CPA has been established. An action on the CPA follows.

2. The rejections and indications of allowable subject matter and subject free of the prior art set forth in the previous Office action, paper no. 11 mailed December 13, 1999 are withdrawn as moot in view of the amendments to the claims. Applicant's remarks have been fully considered.

Informalities

3. The disclosure is objected to because of the following informalities:

(a) Figures 3A and 3B described at page 11 are not in the application and it is not clear that they have been filed.

(b) The use of "SEQUENCE ID NO" as a sequence designator in the specification and claims instead of "SEQ ID NO:" is improper and the disclosure thus is not in compliance with 37 CAR 1.821(d).

Appropriate correction is required.

Rej ction under 35 USC 101: Lack of utility

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

4. Claims 11-14, 38, 39 and 45-49 are rejected under 35 U.S.C. 101 because the claimed nucleic acids are not supported by either a specific and substantial asserted utility or a well established utility. The specification describes the claimed invention at page 23 as "reagents such as polynucleotide sequences derived from a breast tissue of interest and designated BS200". It is stated at least at pages 64 and 65 that assays indicating the presence of BS200 "suggest[ing] a diagnosis of a breast tissue disease or condition, such as cancer". However, at page 57 it is indicated that in a database search the "consensus sequence" (SEQ ID NO:16) was found in only about 39% of breast tissue libraries versus 5% in non-breast tissue libraries, i.e. about 7 times more often in breast than non-breast

tissue. With regard to the occurrence of BS200 in diseased or malignant breast tissue, it is reported at page 68 that PCR products of BS200 were seen in both normal breast and breast cancer tissue, illustrated in Figures 3A and 3B which are not in the application. Therefore, the claimed BS200 nucleic acids do not even have tissue specificity and can be used only to detect BS200 which has not been shown to have any biological significance, i.e., they do not have specific *or* substantial utility. Absent information on the role of the BS200 consensus sequence or the function of the putative protein it encodes the claimed nucleic acids cannot have any "real world" utility.

Rejection under 35 USC 112, first paragraph: Lack of enablement based on lack of utility

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 11-14, 38, 39 and 45-49 are also rejected under 35 U.S.C. 112, first paragraph, as being nonenabled. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above in paragraph 3, one skilled in the art clearly would not know how to use the claimed invention.

Rejection under 35 USC 112, first paragraph: Lack of written description

6. Claims 11-14, 38, 39 and 45-49 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claims encompass a large genus of polynucleotide species the bulk of which are undescribed. The specification discloses the claimed nucleotide sequences, SEQ ID NOS:1-3, 6, 9 and 14-16 as well as the amino acid sequence, SEQ ID NO:31. However, a representative number of polynucleotides comprising sequences having "at least 50% identity" with sequences recited in the claims are not described therein. With regard to claims 11-14, considerable sequence variability would have been expected in view of the absence of any correlation with prior art sequences. Polynucleotides comprising "a polynucleotide sequence of at least about 10 or

12 or 15 or 20 nucleotides are not described in the specification. These sequences are simply mentioned at pages 13-14 and 15-16. Furthermore, the specification fails to teach how to make a representative group of the polynucleotide species encompassed by the claims. Probes and primers are described generically at page 14 and again under "Reagents" at pages 23-24 but no sequences are identified as probes or primers. The references to various known algorithms without a teaching of the one and the parameters to be used with it which provide the polynucleotide sequences of the claims do not constitute a written description of the sequences. Additionally, the references are not incorporated by reference but in any case incorporation of essential subject matter required to describe the claimed sequences and how to make them is improper. The "isolated gene" of claims 38 and 39 is not described. The specification at pages 58-59 identifies a putative open reading frame corresponding to nucleotides 1-1548 of SEQ ID NO:16, the BS200 consensus sequence. However, a full gene, which would be expected to have a complete coding region including start and stop codons, 5' and 3' regulatory elements and other untranslated regions such as introns, is not described. In addition to enablement the first paragraph of 112 requires a "written description". As set forth by the Court in *Vas-Cath Inc. v. Mahurkar*, 19 USPQ2d 1111, the written description must convey to one of skill in the art "with reasonable clarity" that as of the filing date applicant was in possession of the claimed invention. Absent written description of a representative number of the claimed polynucleotides having "at least 50% identity" to a recited SEQ ID NO:, "isolated gene" and polynucleotides comprising "a polynucleotide sequence of at least about 10 or 12 or 15 or 20 nucleotides the specification does not demonstrate that applicant was in possession of the claimed invention at the time the application was filed.

Rejection under 35 USC 112, first paragraph: Lack of enablement of scope of claims

7. Claims 11-14, 38, 39 and 45-49 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for SEQ ID NOS:1-3, 6, 9, 14-16 and 31, does not reasonably provide enablement for polynucleotides comprising sequences having "at least 50% identity to these sequences or their complements or an "isolated gene" or polynucleotides of "at least" 10 or 12 or 15 or 20 nucleotides. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly

connected, to make and or use the invention commensurate in scope with these claims. While the specification does disclose a few additional nucleotide sequences in the Sequence Listing, e.g., SEQ ID NOS: 17-30 which include the prior art primers, SEQ ID NOS:19 and 20 and an 18- and 19mer disclosed as RT-PCR primers, their relationship, e.g., per cent identity or the position of the first nucleotide, to the above-named sequences is not taught. Therefore, one of skill in the art would not have known how to use them. The working examples in the specification teach the use of specific ESTs, cloning and sequencing to obtain the consensus sequence designated BS200 (SEQ ID NO:16). However, the examples do not teach one of skill in the art how to make other nucleic acids of various unspecified sizes and compositions encompassed by the claims. Absent disclosure of a specific method for making a representative number of the large group of sequences encompassed by the claims the citation of prior art alignment algorithms is just that. The level of ordinary skill in the art was high at the time the claimed invention was filed but so, too, was the level of unpredictability. While the prior art teaches generic methods for making and using polynucleotides of various sizes and compositions, neither the BS200 consensus sequence nor its relationship with breast tissue is disclosed. In view of the lack of teaching or guidance in the specification or in the prior art the skilled practitioner would have been required to guess the mind of the inventor to determine the polynucleotides encompassed by the broad scope of the claims. For all of the foregoing reasons, it is clear that undue experimentation would have been required to practice the full scope of the claimed invention. As stated in *In re Wright*, 27 USPQ2d 1510 at 1513 (CAFC 1993),

> Although not explicitly stated in section 112, to be enabling the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without "undue experimentation". *In re Vaeck*, 947 F,2d 488 at 495, 20 USPQ2d 1438 at 1444; *In re Wands*, 858 F.2d 731 at 736-37, 8 USPQ2d 1400 at 1404; *In re Fisher*, 427 F. 2d 833, 839, 166 USPQ 18, 24 (CCPA 1970)

and

> A specification must be more than an invitation to experiment, i.e., applicant may not require persons skilled in the art to perform undue experimentation

to achieve a successful result.

R jections under 35 USC 112, second paragraph: Indefiniteness

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 11-14, 38, 39 and 45-48 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

(a) Claims 11 and 45-48 are confusing in the redundant use of "polynucleotide". It is suggested to change the third "polynucleotide" in claim 11 to --nucleotide sequence--.

(b) Claims 11 and 45-48 lack proper antecedent basis in "polynucleotide" for the sequences represented by their SEQ ID NOS:. It is suggested to change the third "polynucleotide" in claim 11 to --nucleotide sequence--. (Same as above.)

(c) Claim 38 lacks proper antecedent basis for "the amino acid sequence". It is suggested to change "the" to --an--.

(d) Claims 39 is confusing because it is unclear how SEQ ID NO: (*sic* SEQUENCE ID NO) 15 and 16 are to be combined or if they are to be combined for determining the "DNA having at least 50% identity" therewith. It is suggested to change "and" to --or-- or to clarify otherwise.

Rejection under 35 USC 102(b): Anticipation

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claims 11 and 45-48 are rejected under 35 U.S.C. 102(a or b) as anticipated by Hillier et al. (Accession No. AA256868, EST database, 1996) for SEQ ID NO:3 and Matsubara et al. (AC T25603 (Geneseq) WO 95/14772) for SEQ ID NOS: 9, 15 and 16. Each of the references discloses a polynucleotide sequence that "has at least 50% identity" with a polynucleotide of claim 11 identified by its SEQ ID NO: as shown in the sequence

search printouts. Regarding claims 45-48, each of the reference sequences comprises "at least about" 10 or 12 or 15 or 20 nucleotides. Therefore, the references meet the limitations of the claims.

10. Claims 45-48 are rejected under 35 U.S.C. 102(b) as being anticipated by the patent to Agrawal et al. (5,403,709). Agrawal et al. disclose an isolated polynucleotide comprising a polynucleotide sequence of at least about 10 nucleotides that has at least 50% identity with SEQ ID NO:16 (column 7, SEQ ID NO:2 and Figure 1). (See SEQ ID NO:16, first column, third row in the application Sequence Listingat page 97.)

Rejections under 35 USC 102(b)/103(a): Anticipation/obviousness

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CAR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 12-14 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Hillier et al. (Accession No. AA256868, EST database, 1996) and Matsubara et al. (AC T25603 (Geneseq) WO 95/14772). This rejection is based on judicial precedent following *In re Fitzgerald*, 205 USPQ 594 because the references are silent with regard to the embodiments of claims 12-14, *viz.*, how the polynucleotide was made, recombinantly or synthetically, and that it encodes a BS200 epitope. However, these properties are deemed to be inherent in the reference polynucleotides because the reference polynucleotides meet the limitation of "comprising a polynucleotide sequence that has at least 50% identity with" one or more of the sequences recited in claim 11. The burden is on applicant to show that the claimed polynucleotide is either different or nonobvious over that of references.

11. Claim 39 is rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Matsubara et al. (AC T25603 (Geneseq) WO 95/14772). The reference discloses a polynucleotide sequence "comprising DNA having at least 50% identity with [each of SEQ ID NOS:15 and 16]". The rejection is based on judicial precedent following *In re Fitzgerald*, 205 USPQ 594 because Matsubara et al. is silent with regard to the property of being an "isolated gene". However, this property is deemed to be inherent in the reference polynucleotide because the reference polynucleotide meets the limitation of "comprising DNA that has at least 50% identity with [SEQ ID NO:15, SEQ ID NO:16] or complements thereof" wherein the recited "isolated gene" has no defining characteristics of a gene such as encoding an amino acid sequence. The burden is on applicant to show that the claimed polynucleotide is either different or nonobvious over that of the references.

Conclusion

12. No claim is allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephanie Zitomer whose telephone number is (703) 308-3985. The examiner can normally be reached on Monday through Friday from 8:00 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones, can be reached on (703) 308-1152. The official fax phone number for this Group is (703) 308-4242. The unofficial fax number is (703) 308-8724.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

S. Zitomer

Stephanie Zitomer, Ph.D.
June 5, 2000

Primary Examiner